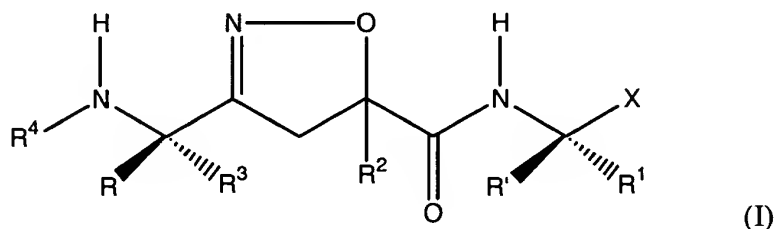


IN THE CLAIMS:

Kindly amend claims 1, 4, 7, and 11-13, as follows:

1. (Presently Amended) An isoxazoline derivative of the formula (I)



in which,

R and R' each independently represents hydrogen, simple alkyl chain (-SAC), simple cycloalkyl (-SCAC), aromatic (-Ar), or simple alkyl chain substituted with aromatic (-SAC-Ar);

R¹ represents -SAC, -SCAC, -Ar, or -SAC-Ar, or represents side chain of amino acids, or - (CH₂)_nCOOZ (in which n is 1 or 2, and Z is hydrogen, -SAC, -Ar, or -SCAC);

R³ represents -SAC, -SCAC, -Ar, or -SAC-Ar, or represents side chain of amino acids;

R² represents -SAC, -SCAC, -Ar, or -SAC-Ar, or represents side chain of amino acids, or represents -(CH₂)_p(O)_mR⁵ (in which R⁵ = -SAC, -SCAC, -Ar, -SAC-Ar; p=0, 1 or 2; and m=0 or 1), or -(CH₂)_qOC(=O)R⁶ (in which R⁶ = -SAC, -SCAC, -Ar, -SAC-Ar; and q=1 or 2);

R⁴ represents

a) amino acid residue in which ① the carboxyl group attached to the chiral carbon of amino acid is bound to the amine group to form an amide bond, ② the chiral carbon of amino acid has either R or S configuration, ③ the amino group attached to the chiral carbon of amino acid is protected by formyl, acetyl, propyl, cyclopropylcarbonyl, butyl, methanesulfonyl, ethanesulfonyl, propanesulfonyl, butanesulfonyl, methoxycarbonyl, ethoxycarbonyl, propyloxycarbonyl, butyloxycarbonyl, methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl,

butylcarbamoyl, dimethylcarbamoyl, diethylcarbamoyl, dipropylcarbamoyl, dibutylcarbamoyl, or cyclopropylaminocarbonyl, or the amino group may be replaced with a hydrogen atom, and ④ the carboxyl group in the side chain may form an ester group with -SAC or -SCAC,

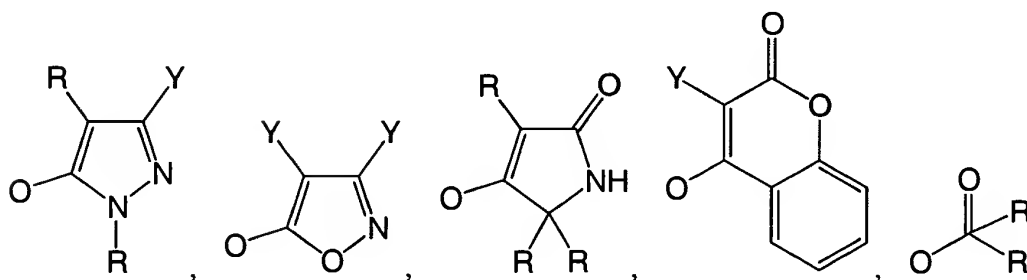
b) $-C(=O)R^7$ (in which $R^7 = -SAC, -SCAC, -Ar, -SAC-Ar$), $-CO_2R^8$ (in which $R^8 =$ hydrogen or R^7), $-C(=O)NR^8R^8$, $-SOR^7$, or $-C(=O)CH=CH-Ar$, or

c) $-(C=O)-L-CO_2R^8$, in which L represents a divalent (=capable of double substitution) linker selected from a group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl, furan, thiophene, diazole (1,2 or 1,3), triazole (1,2,3 or 1,3,4), tetrazole, oxazole, isoxazole, thiazole, isothiazole, diazine, (1,2 or 1,3 or 1,4), triazine, $-Ph(-R^9)-$ (in which $R^9 = H, F, Cl, Br, I, CHO, OH, OCH_3, CF_3, OCF_3, CN, C(=O)Me$), tetrahydrofuran, tetrahydrothiophene, 1,4-dioxane, $-CH=C(R^{10})-$ (in which $R^{10}=H, \text{methyl, ethyl}$), $-CH=CHCH(R^{10})-$, $-CH_2C(=O)CH_2-$, and $-C(=O)CH_2CH_2-$

in cases where R^1 and the adjacent R' , and/or R^3 and the adjacent R are connected to each other to form a cyclic compound, R^1-R' or R^3-R together represents $-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_m-$, or $-(CH_2)_n-NR^{13}-(CH_2)_m-$ (in which $n+m<9$, $R^{13}=-SAC, -SCAC, -Ar, -SAC-Ar, -C(O)-SAC, -C(=O)-SCAC, -C(=O)-Ar$, or $-C(=O)-SAC-Ar$;

X represents $-CN, -CHO, -C(=O)R^{14}$ (in which $R^{14}=-SAC, -SCAC, -Ar, -SAC-Ar, -CHN_2$), $-C(=O)OR^{15}$ (in which $R^{15}=-SAC, -SCAC, -Ar$, or $-SAC-Ar$), $-CONR^{16}R^{17}$ (in which R^{16} and R^{17} each represents $-H, -SAC, -O-SAC, -SCAC, -Ar$, or $-SAC-Ar$), $-C(=O)CH_2O(C=O)Ar''$ (in which $A'' = 2,6\text{-disubstituted phenyl with } F, Cl, Br, I, \text{ or } CH_3$), $-C(=O)CH_2OR^{18}$ (in which R^{18} represents $-SAC, -SCAC, -Ar$, or $-SAC-Ar$), or $-C(=O)CH_2OC(=O)R^{19}$ (in which $R^{19} = -SAC, -SCAC, -Ar$, or $-SAC-Ar$), or

X represents $-COCH_2-W$, wherein W represents $-N_2, -F, -Cl, -Br, -I, -NR^{20}R^{21}$ or $-SR^{22}$ (in which R^{20}, R^{21} and R^{22} each independently represents $-SAC, -SCAC, -Ar$, or $-SAC-Ar$ or R^{20} and R^{21} are connected to form a cyclic compound) or W represents



in which Y represents $-\text{OH}$, OR^{23} (in which $\text{R}^{23} = -\text{SAC}$, or $-\text{SCAC}$), $-\text{C}(=\text{O})\text{R}^{24}$ (in which $\text{R}^{24} = -\text{H}$, $-\text{SAC}$, or $-\text{SCAC}$), $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, $-\text{CN}$, $-\text{NC}$, $-\text{N}_3$, $-\text{CO}_2\text{H}$, $-\text{CF}_3$, $-\text{CO}_2\text{R}^{25}$ (in which $\text{R}^{25} = -\text{SAC}$, or $-\text{SCAC}$), $-\text{C}(=\text{O})\text{NHR}^{26}$ (in which $\text{R}^{26} = -\text{SAC}$, or $-\text{SCAC}$), and $-\text{C}(=\text{O})\text{NR}^{27}\text{R}^{28}$ (in which R^{27} , $\text{R}^{28} = -\text{SAC}$, or $-\text{SCAC}$) and can be mono-or poly-substituted at its maximum regardless of the order and the kinds, the pharmaceutically acceptable salts, the esters and the stereochemically isomeric forms thereof.

4. (Presently Amended) The compound of formula (I) according to Claim 1, in which

- R and R' represent hydrogen,
- R^1 represents $-\text{CH}_2\text{COOH}$, $-\text{CH}_2\text{COOCH}_2$, or $-\text{CH}_2\text{COOCH}_2\text{CH}_3$,
- R^2 represents $-(\text{CH}_2)_n(\text{O})_m\text{R}^5$ (in which $\text{R}^5 = -\text{SAC}$, $-\text{SCAC}$, $-\text{Ar}$, $-\text{SAC}-\text{Ar}$; $n=0, 1$ or 2 ; and $m=0$ or 1), $-\text{SAC}$, or $-\text{Ar}$,
- R^3 represents $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{COOH}$, $-(\text{CH}_2)_2\text{CO}_2\text{H}$, $-\text{CH}_2\text{C}(\text{O})\text{NH}_2$, or $-(\text{CH}_2)_2\text{C}(\text{O})\text{NH}_2$,
- R^4 represents $-\text{C}(=\text{O})(\text{O})\text{R}^{29}$ (in which $n=0, 1$; $\text{R}^{29} = -\text{Ar}$, or $-\text{SAC}-\text{Ar}$), $-\text{SO}_2\text{R}^{30}$ (in which $\text{R}^{30} = -\text{Ar}$ or $-\text{SAC}-\text{Ar}$), or $-\text{C}(=\text{O})\text{NHR}^{31}$ (in which $\text{R}^{31} = -\text{Ar}$, or $-\text{SAC}-\text{Ar}$), or
- X represents $-\text{C}(=\text{O})\text{CHN}_2$, $-\text{C}(=\text{O})\text{CH}_2\text{Br}$, $-\text{C}(=\text{O})\text{CH}_2\text{Cl}$, $-\text{C}(=\text{O})\text{CH}_2\text{OPh}$, $-\text{C}(=\text{O})\text{CH}_2\text{OC}(=\text{O})\text{Ar}''$ (in which $\text{Ar}'' = 2,6\text{-dichlorophenyl}$, $2,6\text{-difluorophenyl}$ or $2,6\text{-dimethylphenyl}$).

7. (Presently Amended) A pharmaceutical composition for treating disease caused by inflammation or apoptosis which comprises as an active ingredient a therapeutically effective amount of an isoxazoline derivative of the formula (I), the pharmaceutically acceptable salts,

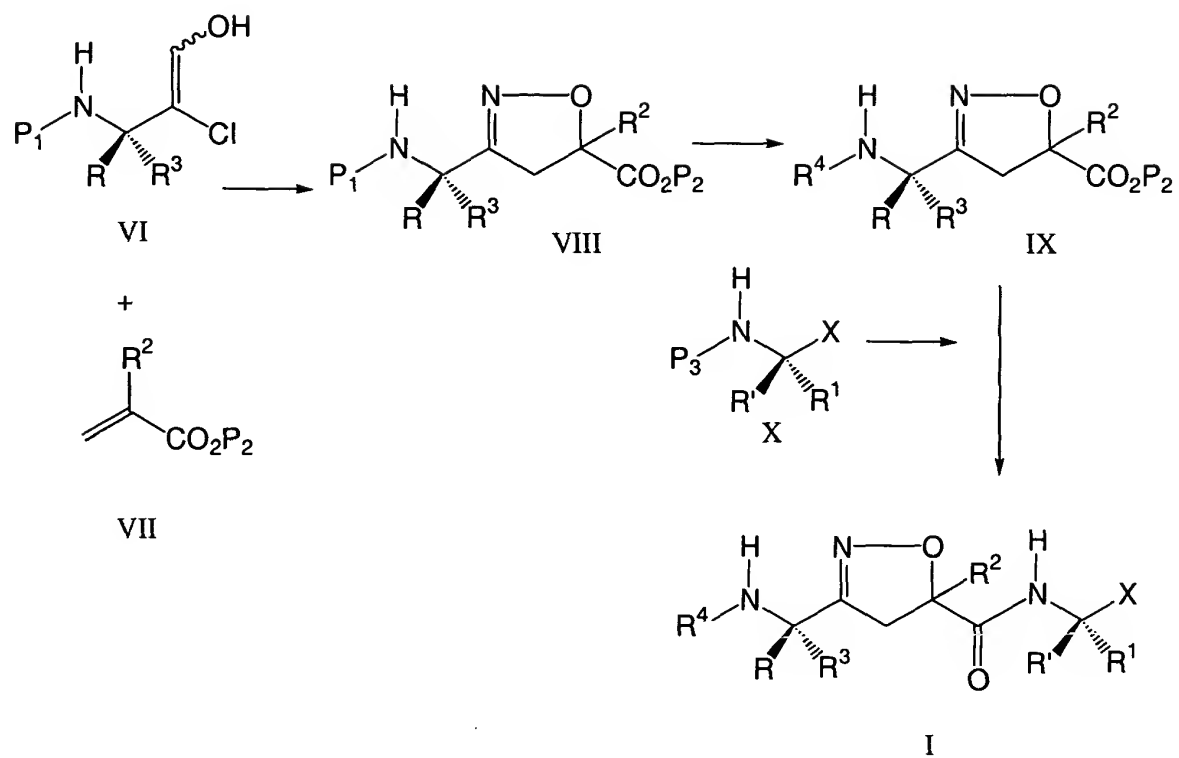
esters or stereochemically isomeric forms thereof as claimed in Claim 1 and pharmaceutically acceptable carrier.

11. (Presently Amended) A method of treating patients suffering from the diseases caused by caspases activation, which comprises a local or systemic administration of a therapeutically effective amount of an isoxazoline derivative of the formula (I), the pharmaceutically acceptable salts, the esters or stereochemically isomeric forms thereof, according to any one of Claims 1 to 5 or the pharmaceutical composition according to any one of Claims 7 to 10.

12. (Presently Amended) A process for preparing a pharmaceutical composition for treating disease caused by inflammation or apoptosis which comprises as an active ingredient a therapeutically effective amount of an isoxazoline derivative and pharmaceutically acceptable carrier, the process comprising the step of:

intimately mixing a pharmaceutically acceptable carrier with a therapeutically effective amount of a compound of formula (I) as claimed in any of Claims 1 to 5.

13. (Presently Amended) A process for preparing a derivative of the formula (I), the pharmaceutically acceptable salts, esters or stereochemically isomeric forms thereof, characterized in that hydroxamoyl chloride (VI) is reacted with acrylate derivative (VII) to give isoxazoline derivative (VIII), and isoxazoline derivative (VIII) is then deprotected and R^4 is introduced therein to give a compound of formula (IX) which is then reacted with a compound of formula (X) and, if necessary, the isoxazoline derivative (VIII) is directly reacted with the compound (X) to give a compound of formula (I), and if necessary, the compound of formula (I) having the protecting group P_1 is converted into other compound having substituent R^4



in which the substituents are the same as defined in Claim 1.